

**WHAT IS CLAIMED IS:**

1. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:
  - 5 a. SEQ ID NO:1;
  - b. a nucleotide sequence encoding amino acid SEQ ID NO:4;
  - c. a nucleotide sequence complementary to SEQ ID NO:1;
  - d. a nucleotide sequence which hybridizes under high stringency conditions to SEQ ID NO:1;
  - 10 e. a nucleotide sequence which hybridizes under moderate stringency conditions to SEQ ID NO:1;
  - f. a nucleotide sequence which hybridizes under low stringency conditions to SEQ ID NO:1;
  - 15 g. a nucleotide sequence which is at least 95% identical to the sequence of SEQ ID NO:1;
  - h. a nucleotide sequence which is at least 80% identical to the sequence of SEQ ID NO:1; and
  - i. a nucleotide sequence which is at least 50% identical to the sequence of SEQ ID NO:1.
- 20 2. The isolated nucleic acid of claim 1 which is DNA.
3. The isolated nucleic acid of claim 1 which is RNA.
4. A vector comprising the isolated nucleic acid of claim 1.
5. A host cell comprising the expression vector of claim 4.
6. The host cell of claim 5 which is selected from the group  
25 consisting of eukaryotic and prokaryotic cells.
7. The host cell of claim 5 which is selected from the group consisting of bacterial, fungal.
8. The isolated nucleic acid of claim 1, wherein the nucleic acid

sequence comprises at least 50 consecutive nucleotides.

9. A vector comprising the isolated nucleic acid of claim 8.

10. A host cell comprising the expression vector of claim 9.

11. The host cell of claim 10 which is selected from the group  
5 consisting of eukaryotic and prokaryotic cells.

12. The host cell of claim 10 which is selected from the group  
consisting of bacterial, yeast, insect, mammalian, and plant cells.

13. The isolated nucleic acid of claim 1, wherein the nucleic acid  
sequence comprises at least 15 consecutive nucleotides.

10 14. A vector comprising the isolated nucleic acid of claim 13.

15. A host cell comprising the vector of claim 14.

16. The host cell of claim 15 which is selected from the group  
consisting of eukaryotic and prokaryotic cells.

17. The host cell of claim 15 which is selected from the group  
15 consisting of bacterial, yeast, insect, mammalian, and plant cells.

18. An isolated nucleic acid variant which comprises the sequence  
of SEQ ID NO:6, and contains at least one single nucleotide polymorphism set  
forth in Table 10.

19. An isolated nucleic acid variant which comprises at least 50  
20 consecutive nucleotides of SEQ ID NO:6, and contains at least one single  
nucleotide polymorphism set forth in Table 10.

20. An isolated nucleic acid variant which comprises at least 15  
consecutive nucleotides of SEQ ID NO:6, and contains at least one single  
nucleotide polymorphism set forth in Table 10.

21. The isolated nucleic acid variant of claim 20, wherein the single  
25 nucleotide polymorphism is selected from the group consisting of T4, T5, T8,

T+1, T+2, R1, Q1, Q2, QR+4, QR+6, QR+7, and U-1.

22. The isolated nucleic acid variant of claim 20, wherein the single nucleotide polymorphism selected from the group consisting of D1, F1, I1, L1, R2, T6, T1, T2, T3, and T7.

5 23. The isolated nucleic acid variant of claim 20 containing at least two single nucleotide polymorphisms selected from the group consisting of:

- a. T+2 and QR+4;
- b. QR+5 and QR+4;
- c. QR+4 and Q+1;
- 10 d. QR+6 and Q2; and
- e. QR+4 and Q2.

24. The isolated nucleic acid variant of claim 20, wherein the single nucleotide polymorphism is selected from the group consisting of:

- a. T5 and T8;
- 15 b. T+2 and QR+4;
- c. T4 and T5.
- d. T+1 and R1 and Q1; and
- e. T5 and R1 and Q1.

25. An isolated nucleic acid variant which comprises the sequence  
20 of SEQ ID NO:1, and contains at least one single nucleotide polymorphism at a site shown in Figure 24.

26. An isolated nucleic acid variant which comprises at least 50 consecutive nucleotides of SEQ ID NO:1, and contains at least one single nucleotide polymorphism at a site shown in Figure 24.

25 27. An isolated nucleic acid variant which comprises at least 15 consecutive nucleotides of SEQ ID NO:1, and contains at least one single nucleotide polymorphism at a site shown in Figure 24.

28. An isolated alternate splice variant which comprises at least one

exon of SEQ ID NO:1 set forth in Figures 9 and 10.

29. An isolated alternate splice variant which comprises at least one exon of SEQ ID NO:1 selected from the group consisting of exons T, R, Q, and U set forth in Figures 9 and 10.

5           30. An isolated alternate splice variant which comprises at least one exon of SEQ ID NO:1 selected from the group consisting of exons A, B, C, D, D', E, F, G, H, I, J, K, L, L2, M, N, O, P, and S set forth in Figures 9 and 10.

31. An isolated alternate splice variant which comprises a sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:350-362.

10           32. An isolated polypeptide encoded by the nucleic acid of any one of claims 1 and 8.

33. An isolated polypeptide encoded by the nucleic acid of any one of claims 18, 19, 25, and 26.

15           34. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a. SEQ ID NO:4;
- b. an amino acid sequence which is at least 80% identical to SEQ ID NO:4;
- c. an amino acid sequence which is at least 75% identical to SEQ ID NO:4; and
- 20           d. an amino acid sequence which is at least 65% identical to SEQ ID NO:4.

35. An isolated polypeptide comprising at least 20 consecutive residues of the amino acid sequence of claim 34.

25           36. An isolated polypeptide comprising at least 7 consecutive residues of the amino acid sequence of claim 34.

37. An antibody or antibody fragment which binds to the isolated

polypeptide of claim 32.

38. An antibody or antibody fragment which binds to the isolated polypeptide of claim 33.

39. An antibody or antibody fragment which binds to the isolated  
5 polypeptide according to any one of claims 34-36

40. The antibody or antibody fragment of claim 37 which is selected from the group consisting of polyclonal and monoclonal antibodies.

41. The antibody or antibody fragment of claim 38 which is selected from the group consisting of polyclonal and monoclonal antibodies.

10 42. The antibody or antibody fragment of claim 39 which is selected from the group consisting of polyclonal and monoclonal antibodies.

43. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- 15
- a. SEQ ID NO:6;
  - b. a nucleotide sequence comprising at least 50 consecutive nucleotides of SEQ ID NO:6; and
  - c. a nucleotide sequence comprising at least 15 consecutive nucleotides of SEQ ID NO:6.

20 44. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- 25
- a. SEQ ID NO:364;
  - b. a nucleotide sequence complementary to SEQ ID NO:364.
  - c. a nucleotide sequence comprising at least 50 consecutive nucleotides of SEQ ID NO:364;
  - d. a nucleotide sequence comprising at least 15 consecutive nucleotides of SEQ ID NO:364.
  - e. SEQ ID NO:365;
  - f. a nucleotide sequence complementary to SEQ ID NO:365;

g. a nucleotide sequence comprising at least 50 consecutive nucleotides of SEQ ID NO:365; and

h. a nucleotide sequence comprising at least 15 consecutive nucleotides of SEQ ID NO:365.

5           45. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a. SEQ ID NO:366;

b. an amino acid sequence comprising 20 consecutive residues of SEQ ID NO:366; and

10           c. an amino acid sequence comprising 7 consecutive residues of SEQ ID NO:M366.

46. An isolated antibody or antibody fragment that binds to the isolated polypeptide of claim 45.

15           47. The antibody or antibody fragment of claim 46 which is selected from the group consisting of monoclonal and polyclonal antibodies.

48. An isolated antisense nucleic acid comprising at least 15 consecutive nucleotides of a sequence complementary to SEQ ID NO:1.

49. An isolated antisense nucleic acid comprising at least 15 consecutive nucleotides of a sequence complementary to SEQ ID NO:6.

20           50. A vector comprising the isolated antisense nucleic acid of any one of claims 48-49.

51. A kit for detecting a Gene 216 nucleotide sequence comprising:

a. the isolated nucleic acid of any one of claims 13, 20, and 27; and

25           b. at least one component to detect binding of the isolated nucleic acid to a Gene 216 nucleotide sequence.

52. A kit for detecting a Gene 216 amino acid sequence comprising:

a. the isolated antibody of claim 42; and

b. at least one component to detect binding of the isolated antibody

to a Gene 216 amino acid sequence.

53. A method of identifying a Gene 216 ligand, comprising:

- 5       a. contacting the isolated polypeptide of claim 35 with a test agent under conditions that allow the polypeptide to bind to the test agent, and thereby form a complex; and
- b. detecting the polypeptide-test agent complex of (a), wherein detection of the complex indicates identification of a Gene 216 ligand.

54. The method of claim 53, wherein the ligand is a metalloprotease inhibitor.

10       55. The method of claim 54, wherein the metalloprotease inhibitor is a proglutamyl peptide analog.

56. The method of claim 55, wherein the proglutamyl peptide analog is an analog of pyroGlu-Asn-Trp-OH or pyroGlu-Glu-Trp-OH.

15       57. A pharmaceutical composition comprising the ligand identified according to the method of any one of claims 53-56, and a physiologically acceptable carrier, excipient, or diluent.

58. A pharmaceutical composition comprising the isolated nucleic acid of any one of claims 1, 8, 13, 43, 48, and 49, and a physiologically acceptable carrier, excipient, or diluent.

20       59. A pharmaceutical composition comprising the vector of any one of claims 4, 9, 14, and 48, and a physiologically acceptable carrier, excipient, or diluent.

25       60. A pharmaceutical composition comprising the isolated antibody or antibody fragment of claim 42, and a physiologically acceptable carrier, excipient, or diluent.

61. A pharmaceutical composition comprising the isolated polypeptide of claim 36 and a physiologically acceptable carrier, excipient, or

diluent.

62. A method of identifying a human Gene 216 or ortholog, comprising:

5 a. contacting the nucleic acid of any one of claims 1, 8, and 13 with a biological sample under conditions that allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and

b. detecting the hybridization complex of (a), wherein detection of the complex indicates identification of a human Gene 216 or ortholog.

63. A method of treating a chromosome 20 disorder comprising  
10 administering the pharmaceutical composition of claim 57 in an amount effective to treat the disorder.

64. The method of claim 63, wherein the chromosome 20 disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

15 65. A method of treating a chromosome 20 disorder comprising administering the pharmaceutical composition of claim 58 in an amount effective to treat the disorder.

66. The method of claim 65, wherein the chromosome 20 disorder is selected from the group consisting of asthma, obesity, and inflammatory  
20 bowel disease.

67. A method of treating a chromosome 20 disorder comprising administering the pharmaceutical composition of claim 59 in an amount effective to treat the disorder.

68. The method of claim 67, wherein the chromosome 20 disorder  
25 is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

69. A method of treating a chromosome 20 disorder comprising administering the pharmaceutical composition of claim 60 in an amount



effective to treat the disorder.

70. The method of claim 69, wherein the chromosome 20 disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

5 71. A method of treating a chromosome 20 disorder comprising administering the pharmaceutical composition of claim 61 in an amount effective to treat the disorder.

10 72. The method of claim 71, wherein the chromosome 20 disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

73. A transgenic mouse whose genome comprises an introduced null mutation in an endogenous Gene 216.

74. The transgenic mouse of claim 73, wherein both alleles of the endogenous Gene 216 of said mouse have been disrupted.

15 75. The transgenic mouse of claim 74, wherein the mouse genome further comprises a human Gene 216 nucleic acid sequence.

76. A method of making a homozygous transgenic knockout mouse comprising:

- 20 a. disrupting an endogenous Gene 216 in mouse embryonic stem cells;
- b. introducing said embryonic stem cells into a mouse blastocyst and transplanting said blastocyst into a pseudopregnant mouse;
- c. allowing said blastocyst to develop into a chimeric mouse;
- d. breeding said chimeric mouse to produce offspring; and
- 25 e. screening said offspring to identify a homozygous transgenic knockout mouse.

77. A method of making a knockout mouse comprising administering the antibody or antibody fragment of claim 47 in an amount effective to disrupt

endogenous Gene 216 polypeptide function, thereby making a knockout mouse.

78. A method of forming a crystal of the isolated Gene 216 polypeptide of claim 36 comprising:

- 5           a. incubating the polypeptide with a solution selected from the group consisting of the solutions in wells 1-30 in Table 1 under conditions to allow crystalization; and
- b. detecting the crystalization in (a), whereby crystalization indicates formation of a Gene 216 polypeptide crystal.

10           79. A method of diagnosing a chromosome 20 disorder, comprising:

- a. contacting the isolated nucleic acid of any one of claims 20-24 with a biological sample under high stringency conditions that allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and
- 15           b. detecting the hybridization complex of (a), wherein detection of the complex indicates diagnosis of a chromosome disorder.

80. The method of claim 79, wherein the disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

81. A method of diagnosing a chromosome 20 disorder comprising:

- 20           a. contacting the isolated antibody or antibody fragment of claim 41 with a biological sample under high stringency conditions that allow the antibody or antibody fragment to bind to an amino acid sequence in the sample, and thereby form a complex; and
- b. detecting the complex of (a), wherein detection of the complex
- 25           indicates diagnosis of a chromosome disorder.

82. A method of determining a pharmacogenetic profile comprising:

- a. contacting the isolated nucleic acid of any one of claims 20-24 with a biological sample under high stringency conditions that allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex;

and

b. detecting the hybridization complex of (a), wherein detection of the complex determines the pharmacogenetic profile.

83. A method of determining a pharmacogenetic profile comprising:

5 a. contacting the isolated antibody of claim 41 with a biological sample under high stringency conditions that allow the antibody to hybridize to an amino acid sequence in the sample, and thereby form a complex; and

b. detecting the complex of (a), wherein detection of the complex determines the pharmacogenetic profile.

10 84. A cell line comprising the isolated nucleic acid of any one of claims 8, 19, 26, and 28.

85. A biochip comprising the isolated nucleic acid of any one of claims 8, 19, 26, and 28.